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April 13, 2001
Date

Karen LePari
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Christopher REEVES, *et al.*

Serial No.: Divisional of 09/410,551

Filing Date: Even Date Herewith

For: POLYKETIDE SYNTHASE ENZYMES
AND RECOMBINANT DNA
CONSTRUCTS THEREFOR

Examiner: Not Assigned

Group Art Unit: Not Assigned

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination, please amend the application as follows:

In the Specification:

On page 1 of the specification, at line 6, please insert the following paragraph:

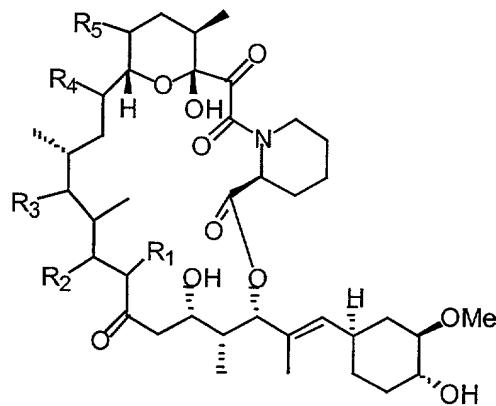
--The present application is a divisional application which claims priority to related U.S. patent application Serial Nos. 60/102,748, filed 2 Oct. 1998; 60/139,650, filed 17 June 1999; 60/123,810, filed 11 Mar. 1999, and 09/410,551, filed 1 October 1999, and PCT/US99/22886, filed 1 October 1999, each of which is incorporated herein by reference.--

In the claims:

Please delete claims 1-17 and 19-20 without prejudice or disclaimer.

Original Claim 18 follows:

18. A polyketide having the structure



wherein, R₁ is hydrogen, methyl, ethyl, or allyl; R₂ is hydrogen or hydroxyl, provided that when R₂ is hydrogen, there is a double bond between C-20 and C-19; R₃ is hydrogen or hydroxyl; R₄ is methoxyl, hydrogen, methyl, or ethyl; and R₅ is methoxyl, hydrogen, methyl, or ethyl; but not including FK-506, FK-520, 18-hydroxy-FK-520, and 18-hydroxy-FK-506.

Please add new claims 21-65 as follows:

--21. The polyketide as in claim 18 wherein R₂ is hydrogen and there is a double bond between C-20 and C-19.

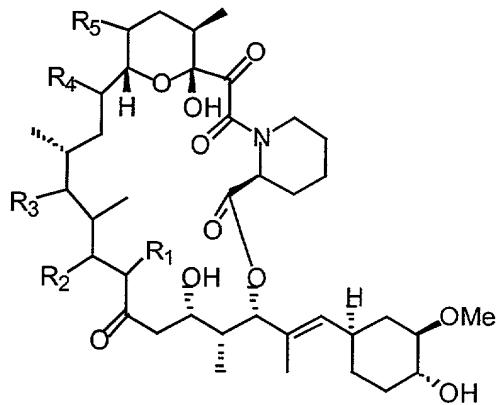
22. The polyketide as in claim 18 wherein R₄ is hydrogen, methyl or ethyl.

23. The polyketide as in claim 22 wherein R₃ is hydroxyl.

24. The polyketide as in claim 18 wherein R₅ is hydrogen, methyl or ethyl.

25. The polyketide as in claim 24 wherein R₃ is hydroxy.

26. A compound of the formula



wherein:

R₁ is ethyl or allyl;

R₂ is hydrogen and there is a double bond between C-20 and C-19;

R₃ is hydrogen;

R₄ is methoxyl, hydrogen, methyl, or ethyl; and

R₅ is methoxyl, hydrogen, methyl, or ethyl; provided that at least one or R₄ or R₅ is not methoxyl.

27. The compound as in claim 26 wherein R₁ is ethyl.

28. The compound as in claim 27 wherein R₄ is methoxyl and R₅ is hydrogen or methyl.

29. The compound as in claim 27 wherein R₄ is hydrogen or methyl and R₅ is methoxyl.

30. The compound as in claim 26 that is 13-desmethoxy-FK-520.

31. The compound as in claim 26 that is 13-desmethoxyl-13-methyl-FK-520.

32. The compound as in claim 26 that is 15-desmethoxy-FK-520.

33. The compound as in claim 26 that is 15-desmethoxy-15-methyl-FK-520.

34. The compound as in claim 26 that is 13,15-didesmethoxy-FK-520.

35. The compound as in claim 26 that is 13,15-didesmethoxy-13-methyl-FK-520.

36. The compound as in claim 26 that is 13,15-didesmethoxy-15-methyl-FK-520.

37. The compound as in claim 26 that is 13,15-didesmethoxy-13,15-dimethyl-FK-520.

38. The compound as in claim 26 that is 13-desmethoxy-FK-506.

39. The compound as in claim 26 that is 13-desmethoxy-13-methyl-FK-506.

40. The compound as in claim 26 that is 15-desmethoxy-FK-506.

41. The compound as in claim 26 that is 15-desmethoxy-15-methyl-FK-506.

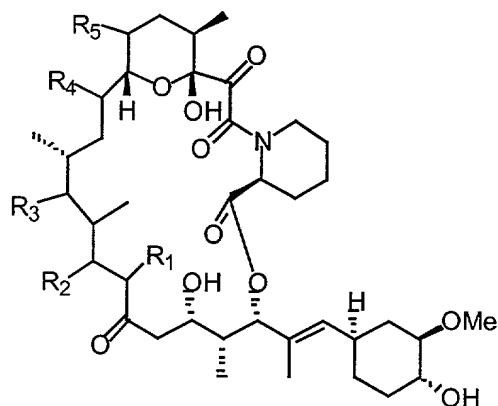
42. The compound as in claim 26 that is 13,15-didesmethoxy-FK-506.

43. The compound as in claim 26 that is 13,15-didesmethoxy-13-methyl-FK-506.

44. The compound as in claim 26 that is 13,15-didesmethoxy-15-methyl-FK-506.

45. The compound as in claim 26 that is 13,15-didesmethoxy-13,15-dimethyl-FK-506.

46. A compound of the formula



wherein:

R₁ is ethyl or allyl;

R₂ is hydrogen and there is a double bond between C-20 and C-19;

R₃ is hydroxyl;

R₄ is methoxyl, hydrogen, methyl, or ethyl; and

R₅ is methoxyl, hydrogen, methyl, or ethyl; provided that at least one of R₄ or R₅ is not methoxyl.

47. The compound as in claim 46 wherein R₁ is ethyl.

48. The compound as in claim 46 wherein R₄ is methoxyl and R₅ is hydrogen or methyl.

49. The compound as in claim 46 wherein R₄ is hydrogen or methyl and R₅ is methoxyl.

50. The compound as in claim 46 that is 13-desmethoxy-18-hydroxyl-FK-520.

51. The compound as in claim 46 that is 13-desmethoxy-13-methyl-18-hydroxyl-FK-520.

52. The compound as in claim 46 that is 15-desmethoxy-18-hydroxyl-FK-520.

53. The compound as in claim 46 that is 15-desmethoxy-15-methyl-18-hydroxyl-FK-520.

54. The compound as in claim 46 that is 13,15-didesmethoxy-18-hydroxyl-FK-520.

55. The compound as in claim 46 that is 13,15-didesmethoxy-13-methyl-18-hydroxyl-FK-520.

56. The compound as in claim 46 that is 13,15-didesmethoxy-15-methyl-18-hydroxyl-FK-520.

57. The compound as in claim 46 that is 13,15-didesmethoxy-13,15-dimethyl-18-hydroxyl-FK-520.

58. The compound as in claim 46 that is 13-desmethoxyl-18-hydroxyl-FK-506.

59. The compound as in claim 46 that is 13-desmethoxyl-13-methyl-18-hydroxyl-FK-506.

60. The compound as in claim 46 that is 15-desmethoxy-18-hydroxyl-FK-506.

61. The compound as in claim 46 that is 15-desmethoxy-15-methyl-18-hydroxyl-FK-506.

62. The compound as in claim 46 that is 13,15-didesmethoxy-18-hydroxyl-FK-506.

63. The compound as in claim 46 that is 13,15-didesmethoxy-13-methyl-18-hydroxyl-FK-506.

64. The compound as in claim 46 that is 13,15-didesmethoxy-15-methyl-18-hydroxyl-FK-506.

65. The compound as in claim 46 that is 13,15-didesmethoxy-13,15-dimethyl-18-hydroxyl-FK-506.--

REMARKS

The instant application generally relates to isolated and recombinant nucleic acids encoding the FK-520 polyketide synthase and its tailoring enzymes, recombinant host cells containing these genes, and use of these nucleic acids and cells in the production of polyketide compounds.

Restriction Requirement

In a communication mailed February 12, 2001, the Examiner determined that the parent of the instant application contained multiple inventions (Groups I-VII). Accordingly, the instant application is a divisional of the parent case, U.S. Serial No. 09/410,551, in which the Applicants elect the invention defined by the claims designated by the Examiner as Group VII.

Claim Amendments

Of the previously pending claims, claims 18 is pending. Claims 1-17 and 19-20 have been cancelled. New claims 21-63 directed to specific compounds defined by claim 18 have been added. No new matter has been added. Support for these amendments are found throughout the specification including pages 82, 127-128 and the examples.

In summary, in response to the Examiner's restriction requirement, Applicants elect in the instant application the invention defined by the claims identified by the Examiner as Group VII. Claims 18 and 21-63 are now pending and believed to define allowable subject matter.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket no. 3006922002610. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: April 3, 2001

By:


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